

U.S.S.N. 10/654,761
Filed: September 4, 2003
AMENDMENT AND
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Remarks

Claims 1-21, 24, 27, 28, 30-37 are pending upon entry of the foregoing amendments.

Applicants thank the Examiner for the indication of allowable subject matter. As detailed below, the foregoing amendments are believed to place all claims in condition for allowance.

Amendments

Claim 1 has been amended to specify that the device further includes a plurality of discrete reservoir caps separating the release system from an environment outside of the reservoirs, and that the method further includes disintegrating one or more of the reservoir caps to expose the release system to the environment, *wherein the disintegration occurs by electrothermal ablation*. Claim 12 similarly has been amended to specify that the device includes a plurality of discrete reservoir caps separating the release system from an environment outside of the reservoirs, and *means for disintegrating one or more of the reservoir caps by electrothermal ablation*. Support for these amendments is found in the specification at least at page 15, lines 3-20; page 18, lines 11-30; and page 24, lines 8-22; and in FIG. 2.

Dependent claim 2 has been re-written for clarity and to have a correct antecedent basis with respect to claim 1 as amended. Claim 10 has been re-written for clarity.

Claims 11, 28, 30, and 31, which the Examiner deemed as being directed to allowable subject matter, have been amended into independent form.

Claims 22, 23, 25, 26, and 29 have been cancelled.

Claim 24 has been amended to specify that the means for disintegrating comprises an electrical input lead and an electrical output lead electrically connected to at least one of the reservoir caps; a power source; and a control means for controlling application of an electric

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current from the power source through said at least one of the reservoir caps, via the input and output leads, in an amount effective to *electrothermally ablate* said at least one reservoir cap. Support for the amendment is found in the specification at least at page 15, lines 3-20; page 18, lines 11-30; and page 24, lines 8-22; and in FIG. 2.

Claim 33 has been amended to depend from claim 30, in view of the amendments to claims 12 and 30.

Claims 7 and 34 have been amended to correct obvious typographical errors of omission.

New claims 36 and 37 have been added. Support for claim 36 is found at least in original claims 20 and 21 and in the description at page 12, lines 12-15; and page 21, lines 13-26, and support for claim 37 found at least in original claims 12 and 33.

Rejections Under 35 U.S.C. § 103

Claims 1-10, 12-18, 22-27, 29, and 32-35 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,797,898 to Santini Jr. et al. (hereinafter "Santini") in view of Rubin et al., "The Potential of Parathyroid Hormone as a Therapy for Osteoporosis," *Int. J. Fertil.* 47(3):103-15 (2002) (hereinafter "Rubin"). Claims 19 and 20 were rejected under 35 U.S.C. § 103(a) as obvious over Santini and Rubin, further in view of U.S. Patent No. 6,264,990 to Knepp et al. (hereinafter "Knepp"). Claim 21 was rejected under 35 U.S.C. § 103(a) as obvious over Santini and Rubin, further in view of U.S. Patent No. 6,011,011 to Hageman (hereinafter "Hageman"). The rejections are respectfully traversed if applied to the claims as amended.

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Applicants' Devices and Methods

For therapeutic efficacy, it is desirable that parathyroid hormone be released in a pulsatile manner with a tightly controlled pulse width. An implantable drug delivery device therefore should be able to release doses of PTH at precise intervals in precise amounts over an extended period of time.

Applicants' devices include a plurality of reservoirs that can be individually activated at precise times to release the PTH. In the specific embodiments defined in claims 1, 12, and 34 (and claims dependent thereon) this reservoir activation, i.e., reservoir opening, occurs with the use of a specific technique: electrothermal ablation. In this electrothermal ablation, a reservoir cap closing off a reservoir opening is ruptured in a manner analogous to the failure of a conventional electrical fuse. That is, sufficient electrical current is passed through the reservoir cap to cause it to heat and rupture.

Santini

Santini discloses multi-reservoir devices for passively or actively controlled drug delivery. Santini describes, for example, active disintegration of reservoir caps by an *electro-chemical* mechanism. In this mechanism, an electric voltage is established between an anodic reservoir cap and a separate cathode through a conductive fluid in contact with the anode and cathode. Application of the voltage causes the anode to oxidize. The oxidized material then dissolves into the conductive fluid, thereby disintegrating the reservoir cap. That process is an entirely distinct mechanism of action compared to electrothermal ablation.

Santini does not disclose or remotely suggest the electrothermal ablation technique or structures therefor. For example, nothing in Santini suggest a device having a pair of conducting

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leads connected to and from each reservoir cap and a controller for selectively delivering an electric current through the reservoir cap *effective to heat and rupture* the reservoir cap. Moreover, electrothermal ablation does not require the presence of an electrolytic fluid to complete an electrical circuit, as does the electrochemical disintegration described in Santini.

Rubin

Rubin discloses the use of parathyroid hormone to treat osteoporosis. Rubin does not, however, suggest administering the parathyroid hormone to a patient with an *implantable* drug delivery device. In fact, Rubin appears to *teach away* from the use of an implantable device for PTH delivery, because Rubin teaches that in the future "oral or transdermal delivery systems may become available" for more targeted delivery of PTH. Nevertheless, Rubin clearly fails to suggest devices or methods that utilize electrothermal ablation to disintegrate reservoir caps to initiate release of PTH, as recited in Applicants' claims 1, 12, and 34.

Santini In Combination With Rubin

It is submitted that one skilled in the art would not have been motivated to combine the teachings of Santini and Rubin in light of Rubin's teaching away from the use of an implantable medical device for administration of PTH. However, *assuming arguendo*, that one skilled in the art would have been motivated to combine the references, the combination nonetheless fails to remotely suggest all elements required by Applicants' claims. In particular, the combination fails to teach any method or device that includes electrothermal ablation of a reservoir cap to initiate release of parathyroid hormone from a reservoir.

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Knepp, Alone or In Combination with Santini and/or Rubin

Knepp discloses stable, non-aqueous protein formulations. Nothing in Knepp supplements the deficiencies of the teachings of Santini and Rubin. For instance, nothing in Knepp remotely teaches *electrothermal ablation* of a reservoir cap to initiate release of parathyroid hormone from a reservoir.

Hageman, Alone or In Combination with Santini and/or Rubin

Hageman discloses protein formulations that include polyethylene glycol as an excipient. Nothing in Hageman supplements the deficiencies of the teachings of Santini and Rubin. For example, nothing in Hageman remotely teaches *electrothermal ablation* of a reservoir cap to initiate release of parathyroid hormone from a reservoir.

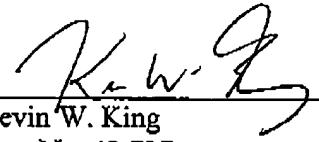
Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully submit that the claims as amended are non-obvious over the prior art of record. All claims are believed to be in condition for allowance. Prompt allowance of each of the pending claims is therefore respectfully solicited.

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The undersigned kindly invites the Examiner to contact him by telephone (404.853.8068) if any outstanding issues can be resolved by conference or examiner's amendment.

Respectfully submitted,



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